Prevention/Repair cream: What's new?

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Summary

Nutricosmeceutical is an artificial word. It tries to describe products that contain ingredients derived from food with high proven efficacy used in cosmetics. There is no legal background for nutricosmeceuticals in contrast to pharmaceuticals, drugs, cosmetics and nutrients which have to meet individual specific regulations in economic regions or countries.

The following major topics will be covered:

- Present situation = Today’s position of these products in the cosmetic field.
- Problems / Open questions = Which relevance have these products to the consumer? Which benefits / problem solution is looked for?
- Solution concept = Which new solutions for the consumer do they offer? What is needed to reach these objectives?
- Future vision: Where will these products lead us? Cosmetics stand for effectiveness but also for well-being i.e. psychological wellness. Holistic concepts, “Body, spirit and soul”, could even be more enlarged.
Riassunto

Nutricosmeceutico è un termine con il quale si cerca di descrivere un prodotto che contiene ingredienti di alta e provata efficacia utilizzabili e utilizzati anche nei cosmetici.

Per questa categoria di prodotti non esiste ancora una regolamentazione giuridica a differenza di quanto avviene per i farmaci per i presidi medici, per i cosmetici o per gli alimenti ed i dietetici.

Vediamo cosa avviene nel mondo a livello giuridico e quali sono le aspettative dei consumatori sulle diverse categorie di prodotti menzionati.

Per i cosmetici, i farmaceutici e gli alimenti, la regolamentazione è chiara in Europa, negli USA, in Australia e nelle nazioni asiatiche, anche se necessitano ancora di una armonizzazione che è però in fase avanzata di realizzazione.

Problemi e quesiti ancora aperti: quale rilevanza hanno questi prodotti per il consumatore?

Come si cerca di risolvere le diverse problematiche?

Oggi, ad esempio, rispetto al passato la domanda del consumatore nei confronti dei cosmetici è notevolmente cambiata. La prevenzione delle patologie è la maggiore richiesta assieme al mantenimento di una cute ed un aspetto generale più giovane.

Quali sono le soluzioni offerte al consumatore?

Quali sono le strade possibili da percorrere per raggiungere gli obiettivi richiesti?

I filtri solari per proteggere la cute sono usati comunemente, ma sempre più vengono utilizzati anche gli antiossidanti di uso più frequente negli alimenti. Inoltre si utilizzano molti principi attivi di uso alimentare quali la vitamina C che debbono essere protetti per svolgere un azione durevole.

Per tutti questi motivi sono stati condotti molti studi sulle nuove tipologie di veicoli, quali la microincapsulazione, in grado di rendere più sicuri ed efficaci i prodotti cosmetici.

Il futuro: come saranno questi prodotti?

I cosmetici saranno sempre più efficaci ed utili per il benessere globale del corpo e dello spirito, ma probabilmente anche dell’anima.
INTRODUCTION

There are clear and legal regulations for cosmetics on an international level and there is no need for a new nutri-cosme-ceutical subcategory.

Nowadays, demands of consumers for creams have dramatically changed in comparison to what they have been for years: prevention and repair have become extremely important. Consumers endeavour to keep a younger looking skin as long as possible. Nutri-based ingredients can help and are therefore integrated in modern cosmetic formulations.

Major challenges for cosmetics are stabilisation/bioavailability, stronger efficacy and guaranteed higher safety. Thus new ideas about innovative encapsulation and/or packaging technologies as well as new test strategies to prove efficacy and safety have been developed. Today, cosmetics not only stand for rational efficacy but also for personal, emotional well-being.

Nutri-based ingredients will inspire and contribute to a more holistic product concept of “Body, Spirit and Soul” in the near future.

The following topics will be covered:

• First, some background information with reference to topical regulations of cosmetics on an international level, especially referring to overlaps between cosmetics, the pharmacy and/or the food sector.
• Second, the relevance of nutri-cosme-ceuticals in the cosmetic field: Which problems do occur and which benefit for the consumer can or do these products offer?
• Third, the 3 major challenges that we face in Cosmetics: the stabilisation/bioavailability of the product, highly proven efficacy and last but not least guaranteed safety.
• Finally, the future aspect: Where can these products lead to?

Definition of the artificial word “nutri-cosme-ceutical”:

“Nutri” means ingredients, derived from food “cosme” means used in cosmetics and “ceutical” means products with highly proven efficacy

The present situation

From a legal point of view a nutri-cosme-ceutical category does not exist.

On an international level in the US there are 4 major categories: cosmetics, over-the-counter drugs, drugs and food.

In Japan there are 4 categories with different legal background in comparison to the US: cosmetics, quasi drugs, drugs and food.

In Europe there are only 3 categories existing, cosmetics, drugs and food, whereas, in Australia the categories are defined as cosmetics, non prescription drugs, prescription drugs and food.

In cosmetics there are various approaches towards harmonisation:

– harmonisation between EC and US
– Japan and Korea opening slowly their legislation, getting also closer to US/EC
– in South America the „Mercosur“.

The process of harmonisation for cosmetic regulations on an international level is running. The position of the cosmetic industry therefore is, that the existing cosmetic regulations are sufficient. There are more products with higher efficacy, there must be a clear balance of efficacy and guaranteed safety, but there is no need of a legal subcategory for cosmetics.

The relevance of nutri-cosme-ceuticals for cosmetics and consumers

Customers have been faced with a dramatic change in living over the last years: The intact environment, clean air and healthy food were more and more replaced by pollution, ozone,
fast food and stress factors. Additionally, people are having a higher life expectancy. Despite all those “negative” life changes, the consumer desires to stay as young as possible as long as possible. To reach this, the consumer requires - better protection / prevention (“An ounce of prevention is worth a pound of cure”) as well as more repair / anti-aging products.

Those benefits can be found in nutri-based products, for example:

In the past, classical UV filters were used for cosmetics as sunburn protection. Nowadays, this is not enough and antioxidants derived from food play an important role as supplements for protection / prevention.

In the past, alpha hydroxy acids were used to get repair effects, whereas now cosmetics already work with products containing vitamin A. Generally, more and more ingredients of food origin are transferred to the cosmetic sector:

- Vitamins: among them vitamin A, C, E and K
- From the enzyme sector: Coenzyme Q 10, Glutathion Peroxidase, Glutation Reductase, Superoxid-Dismutase or Subtilisin
- Plant extracts: oils of green tea, lavender, evening prime rose oil, soy bean derived-, yeast derived- or sugar derived- ingredients which are used e.g. as emulsifiers or emollients, and single ingredients like Alpha Glucosyl Rutin/AGR, Quercit in or other flavonoids.

3 major challenges

To be able to use those nutri-derived extracts or ingredients for products, the cosmetic industry faces 3 major challenges:

- the challenge of stabilisation / bioavailability
- the challenge to prove their even higher efficacy
- the challenge of safety, the must in cosmetics.

Stabilisation / bioavailability

The first challenge was and still is, getting the new innovative nutri-derived ingredients, as e.g. Q 10, Alpha Glucosyl Rutin or vitamin A, stabilised in cosmetic formulations.

To achieve stabilisation, the cosmetic formulators have to be very creative and look for new approaches: such as innovative encapsulations, new formation types (e.g. w/o/w) or they even integrate new packaging technologies such as airless pump systems or 2 chamber packaging (neatly copying the food industry’s müsli-yoghurt packaging = the product is activated on the spot, adding chamber 1 to chamber 2).

Today, formulators can choose from a large selection of highly sophisticated delivery systems which exist at a great variety: Rheological systems, multiple emulsions, molecular – or micro- encapsulations, liposomes or nanobodies are only some of them (see figure 1).

Which delivery system the formulator will use depends on the ingredients and the benefits it should provide the consumer with.

Efficacy

It is remarkable and new, that there are more and more in vitro and in vivo test systems occurring to prove stronger efficacy. The major in vivo tests in cosmetics are e.g. (see figure 2) the hydration / moisture test systems (done by TEWL transepidermal waterloss or Corneometer), the skin surface tests (performed via skin replica, profilometry, etc…), the skin elasticity test (done via Ballistometer, GBE or Cutometer), the antioxidative protection via UPE (Ultraweak-Photon-Emission), etc.
Figure 1: Delivery Systems

Volatile Solvent Carriers
Absorbent Solids
Hydro-/Lamellargels
Rheological Systems
Multiple Emulsions
Liposomes
Nanoparticles
Poros Particulates
Microporous
Microparticles
Molecular-/Micro-Encapsulation
Molecular Film Technology

Figure 2: Proven efficacy: test examples

Skin Elasticity
Ballistometer
GBE
Cutometer

Hydration
TEWL
Corneometer

Skin Surface
Professionometry
Image analysis
Skin replica

Skin Temperature
Thermography

Skin Color
Dermospectrometer

Antioxidative Protection
UPE
**Oxidative Stress: Role of Antioxidants**

Redox Sensitive Signal Transduction

- **H₂O₂, UV**
- **Cell Membrane**, **Cytoplasm**, **Mitochondria**
- **Oxidative stress**
- **Mediators**
- **MAP-Kinase**
- **Nucleus**

**Antioxidants** i.e. **AGR, Q10, Vitamin E**

**Fig. 3**

**Efficacy of topically applied antioxidants**

- Measurement of **Ultra Photon Emission (UPE)**

- **Topical antioxidants (2mg/cm² skin)** Twice a day for 7 days
- **UVA irradiation (50mJ/cm²)** Day 8 50mJ/cm²

- **UPE**
  - **Photomultiplier**
  - **Number of counts**

**Fig. 4**
Prevention is a major target for the consumer. Before going into any detail concerning the antioxidative protection testing we focus on background information referring to both, the ingredients and the test methods. Either are results from body and skin research, based on the free radical theory of aging.

In skin, free radicals can damage the chemical structure and function of lipids, proteins and the DNA. Oxidative stress, induced for example by UV, can activate mediators like the kinase systems: stress signals from the cell membrane are directed to the nucleus via a cascade of enzymatic phosphorylation reactions. There, the transcription of specific stress-associated genes induced, resulting in the expression of stress proteins like ICAM1 or IL1, well known mediators of inflammation. The final result of this oxidative stress response can be seen on the skin as redness, inflammation and / or erythema.

Specific antioxidants as Alpha Glucosyl Rutin, Q 10 or vitamin E counteract these stress-induced transduction cascades and protect skin structures against direct oxidative damages. Thus no redness, inflammation or erythema occurs (see figure 3).

This antioxidative protection can be measured by the non invasive in vitro UPE, the Ultraweak-Photon-Emission measurement. In this test the chemiluminescence is measured before and after UV irradiation. This enables the quantitative evaluation of chemically and / or UV induced oxidative stress. Antioxidants (2 mg / cm2) were applied prior to the UV radiation (50 mJ / cm2). The number of counts of UPE were measured via photomultiplier before and after the radiation (see figure 4).

The product with Coenzyme Q 10 reaches very good results (see figure 5).

The simple rule for the evaluation of the results is: The lower the UPE the better is the antioxidant state of the investigated skin. Q 10 therefore is a valid antioxidant.

To demonstrate a repair, antiwrinkle effect we have used the skin surface image analysis. Ingredients as vitamin A and Q 10, though acting biochemically totally different, have antiwrinkle qualities. The results of a vitamin A containing product, are shown in figure 6: an objective facial lines / wrinkle reduction via image analysis of replicas and parallel a subjective evaluation by an expert grader.

The panel sized 25 people. We see, that this product is very effective in reducing lines and wrinkles. The second example (see figure 7) shows a product containing Q 10: After 10 weeks we have a more than 30% wrinkle reduction. And if you look at longer term results, after 6 months (see figure 8), the skin gets a clear and smooth appearance.

Safety

In cosmetics – other than in pharmacy – safety problems, in other words negative side effects, are unacceptable. Therefore according to the 6th amendment of the EU cosmetic directive, toxicological evaluations for each ingredient are compulsory to ensure full safety of the products. In addition to this, we use more and more in vitro and in vivo safety tests for finished products. There are various in vitro tests existing to prove either the safety like the well known HET CAM, the Red Blood Cell or the vitality of keratinocytes. Other test systems as e.g. the Comet Assay have been used to prove antioxidant efficacy effects but could also be used as a part of a safety test.

Figure 9 shows the in vitro results of the Comet assay of the antioxidant Alpha Glucosyl Rutin (AGR), a plant derived flavonoid. AGR protects significantly the DNA of primary keratinocytes against UVA-induced damage and therefore ensures higher safety requirements.
**Antioxidant efficacy of Q10 containing product**

*in vivo*

Measurement of UVA induced ultra weak photon emission (UPE)

![Graph showing the efficacy of CoQ10](image)

- Control (untreated) vs. CoQ10 (after 7 days of treatment)

**Challenge 2: Proven Efficacy Repair**

"Antiwrinkle effect"

Test Model "antiwrinkle cream" with Retinol

- Objective:
  - Image Analysis
  - Skin replica
- Subjective:
  - Expert grader

![Graph showing objective measurements and expert grader's assessment](image)

Fig. 5

Fig. 6
Reduction of wrinkles after treatment with CoQ10-containing product

Wrinkle Reduction (image analysis, %)

![Graph showing wrinkle reduction over time with CoQ10 treatment vs. control.]

**Fig. 7**

**Challenge 2:**
Proven Efficacy **Repair** Antiwrinkle Effect

Test Model “antiwrinkle cream” with $Q_{10}$

![Comparison images before and after 6 months of treatment with antiwrinkle cream.]

Before treatment  After 6 months of treatment

**Fig. 8**
AGR protects against UVA-induced DNA damage - Comet Assay -

- primary human keratinocytes -
(24 hour preincubation with/without 150µM AGR)

![Graph showing DNA damage comparison between control and 150µM AGR treated keratinocytes.]

Fig. 9

AGR protects against Polymorphous Light Eruption (PLE) and UVA Erythema

**PLE** (Polymorphous light eruption, PLE group)

![Images of skin samples before and after treatment showing effect of AGR and placebo.]

**UVA Erythema** (normal skin, control group)

![Images of skin samples before and after treatment showing effect of AGR and placebo.]

Fig. 10
The in vivo safety test batteries of finished products can be open or closed epicutan (patch) tests, RITPs (repeated insult patch test), ophthalmological tests (eye safety) or in use field studies and – for sun protecting products - phototox- and / or photallergy- studies etc...

Take as an example the design of a clinical photoprovocation study: A placebo formula containing 1 % Vit. E and the verum with 0.25 % AGR included were applied twice a day for 11 days. Both formulae contained no UV-filters. They were applied on skin sites of the upper volar forearms and further there was one site left untreated. There were two groups, one of PLE (Polymorphous Light Eruption) patients and another one of healthy volunteers, the control group. On day 8, photoprovocation tests were conducted applying 60 J UVA/ cm2 skin daily, from day 8 to 11. The scoring of the clinical symptoms were done daily from day 8 to 11.

Figure 10 shows examples of the clinical figure of PLE (PLE group) and of UVA-erythema (control group) on day 11. In comparison to untreated or placebo treated skin sites, AGR can protect impressively against PLE and against UVA-erythema in normal skin, even at these high, repeatedly applied UVA-doses used in this photoprovocation test. This means higher safety to the consumer using this product.

The future vision of nutri-cosmeceutical products

To start with, we all profit from the increasing knowledge of skin and body functions, thus understanding aging processes more thoroughly. Communication systems and mediators to trigger processes will be more and more known.

The second challenge, using nutri-derived ingredient products, is and will be to achieve higher efficacy while safety aspects have to be still guaranteed.

Next, cosmetics in general, but especially the nutri-cosmeceuticals have always 2 bridges to cross: they have to be rationally effective – and give subjective well-being, a totality of psychological aspects. There are still a lot of grey zones. One of them is the measuring of wellbeing. Highly sensitive test methods will have to be developed considering carefully the aspects behind the secret why a consumer states “I BELIEVE in this product”.

Finally, this will also challenge our marketing colleagues making them more aware of getting the right holistic approach to a product: to position, to market and promote it, appealing to consumers on an emotional level.

Therefore a holistic vision based on “body, spirit and soul” is essential - and nutri-derived ingredients inspire this approach.

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References


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